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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,064	11/05/2003	H. William Bosch	029318-0978	6295

31049 7590 11/23/2009

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EXAMINER	
TRAN, SUSAN T	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
11/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/701,064	BOSCH ET AL.	
	Examiner	Art Unit	
	S. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,36-75 and 87-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,36-75 and 87-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/09;8/5/09;9/23/09* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Correction of Inventorship

In view of the papers filed 07/13/09, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by the addition of Rajeev A. Jain, Jon Swanson, Robert Hontz, John G. Devane, Kenneth Ian Cumming, Maurice Joseph Anthony Clancy, Janet Elizabeth Codd, and Gary G. Liversidge to the inventorship of the present application.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 103

Claims 1-14, 16-24, 40-56, 58-72, 74 and 87-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al. US 5,916,596, in view of Stamm et al. WO 98/31360 A1.

Desai teaches a suspended particle comprising active agent coated with a surface stabilizing agent and biocompatible polymer (abstract; and column 7, lines 40-50). Surface stabilizing agent includes protein, casein, peptides, enzymes and combinations thereof (column 15, lines 17-25). Protein is added in an amount ranges from about 0.05%-25% (column 9, lines 19-23). Biocompatible polymer include

chitosan, pectin, cellulose, starch and the like (column 15, lines 1-16). Desai further teaches the active agent has a diameter of not greater less than 1 micron (column 11, lines 10-16). Active agent includes glipizide (column 14, line 30). The examples show the use of active agent in an amount that falls within the claimed range. The particle is to be administered by oral, intravenous, subcutaneous, intraperitoneal, intrathecal, intramuscular, inhalational, topical, transdermal, suppository, pessary, and the like (column 8, lines 17-22). The claimed method is disclosed in columns 9-10, and examples.

Desai teaches glipizide from a list of water-insoluble active agents. However, the desirability for preparing suspended particle of glipizide is known in the art. See for example, Stamm. Stamm teaches a composition having high bioavailability comprising micronized glipizide as active agent suspended in a solution containing surfactant (page 5, lines 32-38; examples 1 and 6). Stamm further teaches active agent in micronized form having particle size below 20 μm. Thus, it would have been obvious to one of ordinary skill in the art to select glipizide as an active agent because Stamm teaches that glipizide is a well known insoluble drug, and that the need to improve dissolution and bioavailability of glipizide is well known in the art, and because Liversidge teaches a formulation suitable for improving bioavailability of a wide variety of active agents including anti-diabetic agents (abstract; and column 3, lines 57-58).

Thus, it would have been obvious to one of ordinary skill in the art to select glipizide in view of the teachings of Stamm, because Stamm teaches the need to improve dissolution and bioavailability of glipizide, and because Desai teaches a

formulation suitable for improving bioavailability of a wide variety of active agents including glipizide.

Claims 1-8, 10, 11, 13-15, 17-24, 40-43, 45-50, 52, 53, 55-65, 67, 68, 70-75 and 87-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liversidge et al. US 5,145,684, in view of Stamm et al. WO 98/31360 A1.

Liversidge teaches a dispersible particle comprising from about 0.1-60% crystalline drug substance, and from about 0.1 to about 90% surface modifier. The particle has an effective average particle size of less than about 400 nm (abstract; column 2, lines 31-43; and column 5, lines 65 through column 6, lines 1-5). Suitable drug substance includes anti-diabetic agents (column 3, lines 57-58). Surface modifier includes hydroxypropyl cellulose (column 4, lines 34-63). Liversidge further teaches a method for preparing the dispersible particle comprising dispersing a drug substance in a liquid dispersion that contains surface modifier to form a premix, homogenizing the premix, and subjecting the premix to grinding media (column 5, lines 41 through column 6, lines 1-17). The obtained dispersion of surface modified drug nanoparticles is combined with pharmaceutical excipient to form pharmaceutical formulation for oral, rectal, injection administration, and the like (column 7, lines 48-64).

Liversidge does not explicitly teach the claimed active, such as glipizide.

Stamm teaches a composition having high bioavailability comprising micronized glipizide as active agent suspended in a solution containing surfactant (page 5, lines 32-38; examples 1 and 6). Stamm further teaches active agent in micronized form having

particle size below 20 μm. Thus, it would have been obvious to one of ordinary skill in the art to select glipizide as an active agent because Stamm teaches that glipizide is a well known insoluble drug, and that the need to improve dissolution and bioavailability of glipizide is well known in the art, and because Liversidge teaches a formulation suitable for improving bioavailability of a wide variety of active agents including anti-diabetic agents (abstract; and column 3, lines 57-58).

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al. or Liversidge et al., in view of Stamm et al. and Baralle et al. GB 2316316.

Desai or Liversidge is relied upon for the reasons stated above. The references do not teach the second population of particle having different particle distribution from the particle distribution of (a). However, bimodal particle distribution is known in pharmaceutical art. Baralle teaches a liquid composition comprising bimodal particle size distribution suitable for parenteral administration (abstract; page 3, lines 23-32; and page 7, lines 3 through page 8, lines 1-23). Accordingly, depending in the release profile desired, the skilled artisan would have been motivated to modify the formulation of Desai or Liversidge to include a bimodal particle distribution in view of the teachings of Baralle. This is because Baralle teaches a bimodal particle distribution is known in pharmaceutical art, because Baralle teaches a bimodal particle distribution that exhibits a useful sustained release profile that is free of serious side-effects (pages 3-4).

Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al. or Liversidge et al., in view of Stamm et al. and Lo et al. 4,389,397.

Desai or Liversidge is relied upon for the reason stated above. The references do not explicitly teach the viscosity of the liquid dosage form.

Lo teaches a low water solubility drug is preferably formulated in liquid dosage form having low viscosity to achieve excellent stability and syringability (abstract; and column 4, lines 10-17). Thus, it would have been obvious to one of ordinary skill in the art to prepare a low viscous liquid dosage form in view of the teachings of Desai or Liversidge and Lo to obtain a stable liquid dosage form suitable for water-insoluble drug. This is because Lo teaches Lo teaches liquid dosage form having high viscosity will cause precipitation, irritation and tissue damage at the injection site (column 1, lines 25-29), because Lo teaches a low viscosity liquid dosage form overcomes the disadvantages in the prior arts and exhibits excellent syringability (ID).

Response to Arguments

Applicant's arguments filed 07/13/09 have been considered but are moot in view of the new ground(s) of rejection.

Applicant argues that Liversidge discloses a laundry list of drug categories and illustrative species of drugs without any teaching or suggestion to select an anti-diabetic agent. Rather, Liversidge discloses anti-cancer drugs and steroids in preferred embodiments.

However, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Liversidge is cited in view of Stamm for the suggestion to select an anti-diabetic agent such as glipizide.

Applicant argues that Stamm fails to teach a nanoparticulate glipizide composition.

However, in response to applicant's argument, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). It is however, noted that Stamm teaches glipizide in micronized form having particle size below 20 µm (page 5, lines 32-38; examples 1 and 6).

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 07/13/09, 08/05/09 and 09/23/09 prompted the new ground(s) of rejection presented in this Office action. Accordingly,

THIS ACTION IS MADE FINAL. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615